SIGMA XI QUARTERLY

VOL. XXI | DECEMBER, 1933 | NO. 4

THIRTY-FOURTH CONVENTION

BOSTON, DECEMBER 28

TODD ON

"HUMAN BODIES AND HUMAN BEINGS"

SMITH ON

"EVOLUTION OF THE KIDNEY"

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Published at Burlington, Vermont, by the Society of Sigma Xi

ANNUAL SUBSCRIPTION $1.00 SINGLE COPY 25 CENTS

Application for transfer from Easton, Pa., to Burlington, Vt., pending. The Sigma Xi Quarterly is published at 187 College St., Burlington, Vt., in March, June, September and December.

Change of address of chapter members and associates should be communicated to chapter secretaries and to the National Secretary.

Subscriptions should be sent to the National Secretary, Edward Ellery, 187 College St., Burlington, Vt., or Union College, Schenectady, N. Y.

Manuscripts should be sent to the National Secretary at Schenectady, N. Y.

SIGMA XI QUARTERLY

Vol. XXI DECEMBER, 1933 No. 4

THE THIRTY-FOURTH CONVENTION

The annual convention of our great society will be held in Boston, Thursday, December 28, 1933. The program of events is as follows:

4 P.M. The Business Session.
Parlor A, Hotel Statler.
6.30 P.M. The Buffet Supper. Hotel Statler.
8.30 P.M. The Twelfth Annual Sigma Xi Lecture. Ballroom, Hotel Statler.
Speaker: PROF. HENRY E. SIGERIST, Johns Hopkins University.
Subject: THE FOUNDATION OF ANATOMY IN THE RENAISSANCE.

THE BUSINESS SESSION

Following are the important items of business at present on the agenda. Chapters are especially urged to notify the National Secretary, before December 20, of additional matters which chapters may wish to bring to the attention of the convention. The national officers desire to find place in the program for all business associated with the progress of the Society.

1. Consideration of formal printed petitions for charters for chapters:
   (a) Tulane University.
   (b) Massachusetts Institute of Technology.

2. Proposed amendment to the Constitution: Shall the Executive Committee be empowered to elect as associates of the Society promising students in institutions where there is no chapter?

3. The semi-centennial program.

4. Sigma Xi certificates of award for research. Report of Committee of Award.

5. Election of officers.

The convention will be called upon to nominate and elect a president, secretary and treasurer for the ensuing biennium, a member of the executive committee for a term of five years to succeed Professor Lloyd, whose term expires in January, 1934, and a member of the alumni committee for a term of five years to succeed Doctor Hirshfeld, whose term expires this year.

The nominating committee, appointed by President Wilson, is as follows:

Prof. Harlow Shapley, Harvard, chairman.
Prof. J. A. Anderson, California Institute of Technology.
Dean E. A. Bessey, Michigan State College.

Chapters are asked to make suggestions of nominees to the committee.

IMPORTANT

Chapters are asked and urged to select as their delegates members who will be sure to be able to attend the business session of the convention. It is the opinion of the national officers that wherever possible the delegates should be members whose connection with the chapter is somewhat permanent, who have had experience in chapter and society affairs, and whom the chapter might choose as its representative on the National Committee of Arrangements for the Semi-Centennial. Each chapter is entitled to a representation of three delegates.

Will chapter secretaries send to the National Secretary the names of their delegates as soon as they are appointed, and provide each delegate with a statement of his appointment for presentation to the Committee on Credentials at the opening of the Convention.

HUMAN BODIES AND HUMAN BEINGS*

T. WINGATE TODD

AKHENATEN

A Pharaoh called Akhenaten lived in the Eighteenth Dynasty, which means about 1500 B. C. He was clever, fearless and courageous. He came to the throne in childhood and, with the enthusiasm and lack of judgment characteristic of inexperience, in the sixth year of his reign, publicly declared his adhesion to the cult of Aten and in this religious fervor, regardless of the fact that the whole social life of his capital was bound up in the worship of Amen, disbanded the priests and confiscated their revenues. For this he became abhorrent to his people who desecrated his mummy after death and heaved his dishonored body into a disused tomb originally built for his famous mother, Queen Ty. Much legend centered about this Pharaoh who died at an early age. His body was found by Arthur Weigall in searching for the Queen at the instigation of Mr. Davis of Rhode Island. The scientific controversy concerning his age at death drew anatomists, archeologists and historians into the discussion and was the initial stimulus which set my own efforts toward the elucidation of skeletal features by which the actual age at death might be identified.

When I came to Cleveland twenty years ago I set to work to gather the skeletons, clinical and social histories of the unclaimed dead so that, in the course of time, we accumulated records of over two thousand people.

With the aid of my students and assistants I began to identify and classify the skeletal features associated with age. We found them in the union of epiphyses, the contours of articular surfaces, the character of suture lines and the textures of bone.

It fell to the lot of Dr. P. H. Stevenson of Peiping Union Medical College to investigate the union of epiphyses. Stevenson found that the order of union is invariable, that the current text-book descriptions are invalid and that there is a definite age-relationship in epiphysial closure which can be set forth in graphic form now known as Stevenson's keys. Setting the observations of epiphysial union as seen in Akhenaten's skeleton beside these keys it is plain that the Pharaoh died at twenty-two years of age. But the historians wanted him to be at least thirty and it was suggested by Elliot Smith that we had misread the signs of age, that Akhenaten was suffering from dystocia adiposgenitalis, a disease which delays epiphysial union, and that Akhenaten was really perhaps as much as thirty-six when he died. It was clear that we must know more about the signs of health and disease in the skeleton.

THE BLACKSMITH OF ERIE STREET

Now there was, on my arrival in Cleveland, a blacksmith of very peculiar form. He was semiparalytic on the left side; his legs were long and shambly; his voice unbroken and his face devoid of hair. He had all the features which we recognize as eunuchoid. In the course of time his body came to swell

*A paper read before the Pittsburgh Chapter.

the growing numbers of those who rest in the catacombs of our Permanent Morgue and when we commenced to examine the skeleton we found that despite an age of thirty-nine years the epiphysial union was delayed. The actual stage of closure corresponded on Stevenson's keys with an age of nineteen years. But time had left indelible and indisputable evidence of his condition in his bones. This was not a simple delay in epiphysial closure. The ununited diaphyso-epiphysial planes were wildly pathological. The ends of the shafts showed no simple billowy pattern as those do, of which the epiphyses are not united, but a bizarre cauliflower-like mass, a sort of petrified "proud flesh" in bone. And we therefore described the condition as lapsed union. Not once but many times we have found this appearance in the human skeleton. It can be recognized in the roentgenograms of patients who are still alive. Once again indeed we were baffled by the rejoinder, perfectly logical in scientific discussion, that the theme of lapsed union was not proved. It might be that we had stumbled upon a definite pathological condition of which these cauliflower-like bone-ends are characteristic and that it is no true consequence of simple delay in union. We had not experimentally proved our case. We knew we were on the right track and that patience in the accumulation of data would make our proof complete. Meantime we had learned a most important truth, namely, that age-relationship of skeletal progress can be interfered with by general constitutional causes.

THE CORNELL SHEEP AND THE WISTAR RATS

It was almost at the beginning of the investigations just described that I inquired of Prof. Sutherland Simpson if I could have the privilege of investigating the skeletons of the sheep which were the subject of his studies in hypothyroidism. Professor Simpson arranged that these skeletons should be sent to me together with the skeletons of the normal control twins. Altogether he and Doctor Liddell sent me seven sheep thyroidectomized at one month of age and two thyroidectomized at two and at three months, respectively. These animals together with their controls were of the utmost importance. I already knew something of the order and nature of epiphysial union in mammals, having studied over 1,000 young mammals comprising all the natural orders.

The thyroidectomized sheep were all dwarfs, but, more than this, they showed delayed epiphysial union. As a rule a sheep from which the thyroid gland is extirpated dies of respiratory disorder within two years but some of the animals lived longer and one survived the operation as long as five years. It would be incorrect to say that union of epiphyses was inhibited. The successive stages of union were greatly delayed and eventually the urge to union faded out, so that, according to the length of survival after the operation, the site of union showed progressive aberrancy culminating, if the sheep lived long enough, in the same general features as were displayed in the skeleton of the Erie Street blacksmith.

We had then attained experimentally the object of our search, namely, the practical inhibition of epiphysial union. But the result was not what we had forecast. Inhibition was not characteristically a result of defective gonadal development. It could equally well be brought about by hypothyroidism. It was actually produced by slowing up the process until the impetus to close

faded out. This investigation shed new light upon the non-specificity of interruption in developmental growth. It indicated pretty clearly that the energy of developmental growth is applied to particular phases of the process at successive periods in the life-span. When the normal date for exhibition of a particular phase is past that phase is likely to remain defective throughout life. If union lapses for a long enough period it cannot be brought about for there is no longer any response to stimulus possible in the organism.

At the time we were carrying out these observations on sheep Alden B. Dawson was investigating epiphysial closure in the Wistar rats. He found that, even in quite old rats, rats namely of five years, in this colony, the epiphyses of the upper humerus and femoral head did not close. Dawson's findings were confirmed by H. A. Harris of University College, London, on other domesticated white rats. And Hinton of the British Museum announced that, in Arvicola, a field mouse, the epiphyses never close.

Now I had examined the bodies of about 150 wild rats (Muridæ) and it was perfectly clear from my investigations that, in the wild state, the epiphyses do close and that they unite in definite order as they do in other mammals.

Hinton's conclusions were soon explained. The animals he examined, though they numbered several thousand, were the skeletons of mice overwhelmed by disaster while in migration. All were of about the same age and were at the stage of epiphysial union. They were victims of a vernal urge. There were no old animals among them. This statement is, however, not absolutely true. One single aged animal was found with arthritic lipping and union of epiphyses, among the thousands of young ones, to prove the justice of my contention.

Dawson's and Harris' findings were less easily disposed of. At my suggestion Dawson made a histological study of the epiphyses which did not close and he discovered that these ununited epiphyses display all the characteristic features of the blacksmith's epiphyses, affecting, however, only the two particular epiphyses noted. Although the Wistar Colony animals were carefully reared and fed and appeared normal in all physiological and outward clinical respects they display this aberrancy in upper humerus and femur. Our next conclusion was therefore that the skeleton is a very delicate indicator of disturbance in the chemical balance of bodily metabolism. Animals that appear clinically healthy and physiologically normal may, like many well human beings, still be deficient in perfect well-being.

So back we come to Akhenaten. The proof of actual delay in epiphysial union may be sought in the characteristic appearance of the sites of epiphysial union. Since the epiphyses of the Pharaoh show no aberrancy whatever in structural detail he cannot with justice be claimed the victim of any disorder which disturbed developmental growth. Of course, by the time we had finally proved our point the discussion of Akhenaten had faded from popular attention: the historians had settled into smug complacency in their apparent victory.

THE BULUWAYO SKULL

Although Akhenaten had become a back number, the subject of human developmental growth took a new turn from the discovery in 1924 of the skull in a cave of the Broken Hill mine near Buluwayo, Rhodesia. The problem

before the anthropologists was a decision upon the zoological standing of this fossil. It was either a man very similar to the Neandertal type in Europe or an extinct higher primate, subhuman in character. This fossil skull has been extensively studied by Pycraft and other anthropologists with conflicting conclusions. Every investigator, however, missed the most significant feature, namely, the closure of coronal suture and patency of lambdoid.

It so happened that Lyon and I had worked over the suture closure of more than 1,000 skulls in our collection, all of known individuals whose age was recorded and confirmed by a study of the skeletons. As with epiphysial union we found a definite order in sutural closure invariable in both whites and negroes, namely, sagittal, coronal and lambdoid in that order, at the approximate respective ages of thirty, thirty-five and forty-seven years. This finding was contrary to the accepted conclusions based on scattered and thoroughly unreliable observations of previous workers who had contended that in the negro the lambdoid closes before the coronal suture, a supposition which was claimed to distinguish him from the white man. When we published our findings no one took them seriously because we qualified them with the reservation of lapsed union, a phenomenon characteristic of suture closure in man alone among mammals. Further, very few investigators took the trouble to look inside the cranium where the suture closure pattern is best exemplified. Lapsed union is far more frequent on the outside of the human cranium.

If lapsed union occur externally only, the suture margins of adjacent bones are closely knit. If it occur throughout the skull wall, and is evident on both surfaces, the endocranial sutural edges are heaped up and inverted in a manner which reminds one forcibly of the "clawed" appearance of the eyelids of trachoma.

From our studies in lapsed union of epiphyses we had learned that delay in closure extends long beyond the date at which it should take place and results in permanent patency. This marked tendency toward lapsed union of cranial sutures which characterizes mankind accounts for the so-called individual variation in spread of closure over the sutures of the cranium, for it is true that some quite aged skulls show an almost complete absence of sutural closure. We were, therefore, even when we published our results, quite reconciled to the total rejection of our conclusions. And in this expectation we were not disappointed. We had learned another important and fundamental fact of developmental growth, namely, that individual variation is not to be interpreted as something inherent in the organism but a phenomenon for which there must be a definite cause, a cause which can be found if the search be meticulous enough.

Bolk indeed, working upon a far larger selection of children's skulls from the Amsterdam Necropolis showed that individual variation is so great that union of sutures may occur in early life. And he made the observation, the significance of which escaped him but is apparent from our studies described below, that if "premature" union occur it takes place by the age of seven years.

Now a team of workers in this laboratory undertook the study of cranial suture closure in mammals, similar to the investigation of epiphysial closure made by myself. Among these workers Krogman elected to study suture closure in anthropoids and Old World apes. He found in the first place that these animals evince the regular mammalian order of suture closure, namely, sagittal, lambdoid and coronal. This is the sequence hitherto erroneously claimed for the negro. But Lyon and I had shown quite conclusively that man's closure pattern is sagittal, coronal, lambdoid in that order. The Rhodesian skull happens to be at the stage when sagittal and coronal sutures are closed and lambdoid is still patent. The inference is plain. This skull is that of a man despite the anthropoid semblance, of a man moreover between thirty-five and forty-five years. Our anthropological colleagues throughout the world discounted all this work and continue to surmise upon the zoological affinities of this quite definitely human relic.

DARNLEY

The complete rejection of all our work on the suture closure pattern was demonstrated in the controversy over the skull now in the College of Surgeons, painstakingly identified by Karl Pearson by its history and fit to the portraits as that of Henry Darnley, husband of Mary Queen of Scots. This skull was laid before me by Sir Arthur Keith as an "unknown" with the request that I identify the age. Discrimination was not difficult after a detailed examination of sutural lines and other age characteristics and I gave a diagnosis of twenty-two years. With that observation my participation in the investigation terminated. I was then informed that this was Darnley's skull. We know from history that the unfortunate man was killed at Kirk O'Fields where Edinburgh University now stands, at the age of twenty-two. But my identification remains unnoticed in the wordy battles over the authenticity of the skull. Anthropologists are still too limited in experience and understanding of developmental growth to discriminate between well-founded observations and mere assumptions.

MARGARET OF ANGOULÊME

One must not, however, cavil at the slowness of penetration by new ideas. The time-lag of scientific conservatism is notorious, but in the end careful and thoroughly substantiated observations find their usefulness. And within the last few months our ten years' study of cranial features has met its proper recognition.

In June, 1930, my colleague, Prof. R. Anthony, sent to me some excellent photographs of a skull lacking the face found in the crypt of the Cathedral of Lescar in the Pyrenees. This cranium, damaged though it was, carried enough evidence to permit identification of age. Four of us in the laboratory, including Krogman and myself, assessed its age features. It was clearly the remains of a woman about fifty-five years of age. Unequivocal evidence limited its possibilities to a minimum of forty-seven and a maximum of sixty-four years. Finer discrimination pointed to fifty-five with the possibility of a few years on one or other side of this mean value. We did not know, at the time of

examination how significant our finding was. The skull could belong only to one of two ladies, Margaret of Angoulême, the authoress of the Heptameron, or her mother-in-law, Catherine de Foix. History and circumstantial evidence strongly indicated the former. The anatomical evidence fixed the identification and Professor Anthony, for the first time in anthropological investigation, made full use of the new knowledge on age characters in skull and skeleton gathered in this laboratory during the past twenty years.

PRINCIPLES OF SKELETAL DEVELOPMENTAL GROWTH

With Margaret of Angoulême we may take leave of the more academic aspect of this investigation. And, in so doing, a summary may be conveniently made of the general principles which have emerged.

(1) There is a definite sequence in union of both epiphyses and cranial sutures. The epiphysial sequence is invariable in health and disease alike. The sutural sequence is occasionally modified by "lapsed union" or "premature union."

(2) There is an age-relationship in epiphysial and sutural union which is disturbed by any influence which interrupts, delays or inhibits developmental growth. These influences are non-specific in their effect.

(3) So-called individual differences in age-relationship are not inherent in the organism but induced by specific causes.

(4) The energy of developmental growth is expressed in definite demonstrable stages at particular periods of the life-span.

(5) If delay interferes with the completion of a stage at the appointed date it is likely to be permanently omitted from the pattern of developmental growth.

(6) So-called recovery is usually not a restoration but a reconstitution.

THE GRADE SCHOOL PATTERN

In 1926 the Cleveland Health Council asked if our investigations had reached a stage where they could be set to practical use in the quantitative assessment of developmental growth in children, offering to subsidize an exploration along this line of endeavor if we were ready to put our researches to that test. At the same time the Board of Education offered the facilities of Stearns Road Grade School should we decide to comply with the offer of the Health Council. We accepted the challenge and commenced the series of studies on child growth and development which is now carried on under the title of the Developmental Health Inquiry.

It is a very stimulating and healthy thing that when a Foundation gives money to a scientific endeavor it should require returns almost at once. I feel that we are apt to magnify indecision in renaming it conservatism. However, we never had the chance to fall into philosophic error for, when we had examined 150 children of both sexes between seven and nine years of age the Health Council asked for a report upon the work and named a date three months from the commencement of the study. This was a challenge more serious than the former one. There was obviously no time to complete a full study even of the records. A start had to be made somewhere. We had

planned the work as a study in growth and development, using the skeleton as an index of physical developmental growth on the hypothesis that skeleton, like muscles, blood and respiratory capacity must share the general bodily curve of growth if not of progress to maturity. To this end we had devised a schedule of measurements of growth including height and weight, and had also carried out a series of roentgenograms of hands, elbows, shoulders, feet, knees and hips to give us a picture of developmental progress.

In order to fulfill our duty to the Health Council I decided to survey height and weight as measures of growth together with roentgenograms of knees as an index of physical development. Norms of height and weight in relation to age were available in the Baldwin-Wood standards. The next step was to inquire how closely roentgenograms of the knee could indicate the actual age of the child.

Dr. Joseph D'Errico, Jr., bore with me the burden of this first investigation. We gathered the roentgenograms by yearly intervals of age and closely studied each series, using boys alone in our search for significant data.

It was soon clear, as we had predicted, that the roentgenograms did indeed demonstrate a progress in maturity, indicated by the increasing penetration of the epiphysial cartilage by bony tissue whereby the ossifying epiphysis gradually took on more and more of the features to which we are accustomed in the conformation of the articular ends of femur and tibia in the adult.

At seven years a majority of our all-too-small group showed a tibial epiphysis in which ossification had not yet progressed to the stage when articular outline could be seen. The end of the shaft, moreover, showed an increased density to a depth of some 3 mm. from the surface of the diaphyso-epiphysial plane.

At eight years this increased density had disappeared and the excavations representing the articular surface of tibial tuberosities were outlined in bone.

At nine years we found no very significant changes in tibial epiphysis but the ossified medial condyle of the femur was distinctly larger in vertical direction than the lateral condyle.

We soon found that these simple definitions were insufficient to describe all the fine gradations of distinction which could be described only by actual comparison, with each other, of roentgenograms at different ages.

We then took one roentgenogram of each group which most nearly represented the mode in developmental progress for that group and used it as a standard assessing by it the remainder of each group as of modal (average), accelerated or retarded development.

Having made our arrays in terms of developmental progress we gave each knee, as representing the child on whom the roentgenogram was made, a comparative age evaluation. To our chagrin, at first, we found that development and chronological age did not coincide. Many of our seven-year-olds fell far below the standard for seven years. Some of our nine-year-olds registered a far greater development than the nine-year standard. And our eight-year-olds were distributed over, and in some instances below or above, the range represented by our three standards for seven, eight, and nine years,

respectively. A bare majority of each group did indeed cluster around the standard for that age and this gave us courage to continue if not great confidence that we were upon the right track.

Since it was evident that we could not align the developmental progress of knee epiphyses with chronological age we endeavor to ascertain its relationship to stature and weight. In this comparison we found less correspondence than with age though weight seemed to be a little more closely correlated than height. About half these boys were of native American stock and the other half the children of immigrant Sicilians. These latter were shorter though stouter than the former. As yet we had no suggestion as to the meaning of our findings and indeed no indication that they were at all representative of what we should ultimately find in larger samples. Statistical reduction was out of the question as the groups were too small. Of our seventy-five boys we were able to discover the birth certificates of only some forty-five. Without a birth certificate we felt it too hazardous to take the age given by the school record as indubitable. In this we were a little too meticulous as later experience proved. There are indeed some erroneously stated ages but they constitute only a small minority. However, we did not know this at the time and preferred to exclude rigidly all children from our initial survey when we had not the fullest information on age which modern city records can give.

Our three groups of boys dwindled therefore to a paltry fifteen per group. We expected that our results on so small a series would make no impression on our judges but we drew up suggestions for our guidance in dealing with samples of more convincing size and later investigation has confirmed their essential truth. Our long apprenticeship in the study of the skeleton saved us from error.

These suggestions were:

(1) There is no necessary relationship between growth in dimensions and progress in developmental maturity.

(2) There is a relationship between chronological age and developmental maturity but this relationship is not a simple one. It is subverted by conditions of which we as yet knew nothing.

(3) Individual variation seems skewed so that there are more children who have not reached the mode of developmental progress than there are of children who have surpassed it.

The 800 children of Stearns Road School, ranging from five to twelve years with a scattering few beyond both age limits, were examined at least twice in 1926 and 1927. Some were examined three or four times. Ten roentgenograms were made at each examination. For five years we studied the 20,000 roentgenograms. Assessments of developmental progress were made independently by never less than four and usually by eight observers all carefully trained by long experience. The results were statistically treated for reliability and uniformity of assessment. The correlation-coefficient of assessment was found to be about 0.9. Hands, elbows, knees, feet and shoulders were investigated separately. Results were pooled and the children studied as

individuals and in the end we felt confident of our results. These may be summarized in the following manner:

(1) Modal evaluations of developmental progress by six-month intervals in age between five and twelve years can be obtained from roentgenograms of epiphyses especially made by standardized technique for that purpose.

(2) To obtain a proper evaluation attention must be directed to all the epiphysial areas mentioned.

(3) Developmental progress in knees and feet is more closely related to stature. Developmental progress in hands and elbows is more closely related to chronological age.

(4) Separate standards must be utilized for boys and girls.

(5) Fewer boys than girls exceed the mode in development. More boys than girls are retarded below the mode.

(6) Girls at five and twelve years are somewhat more advanced in developmental progress than boys. In the approximate middle of the range, namely, about nine years, there is little sex difference.

(7) Sicilian children show no real racial difference in developmental progress from those of American-born parents.

(8) Negro children show no real difference in developmental progress from whites, but there are more negro children retarded below and accelerated beyond the mode than there are of white children.

(9) The children accelerated beyond the mode in developmental progress are usually, but not always the bigger, heavier, more robust. Those retarded below the mode are usually small, underweight and enfeebled.

(10) The roentgenogram affords fresh insight into the state of developmental health and amplifies such other determinations as height, weight, muscular power and vital capacity.

(11) Further elucidation of the meaning of these relationships can be secured only by a knowledge of medical, social and economic history of the child together with a study of his diet and of his psychic and emotional development.

ANOMALIES IN DEVELOPMENTAL GROWTH

From our studies on Stearns Road Grade School children we were beginning to get some direction for measurement of developmental growth and we therefore sought clear instances of nutritional deficiency in the hope that children of this category would serve to emphasize, by contrast, the principles which we were seeking. Miss Buchanan at once sent us the twenty children at the time in the Fresh Air Camp for undernourished children. These we graded on height, weight, muscular power and roentgenographic development. From these we learned how marked can be the asymmetry of developmental growth. Usually height and weight bear a certain relationship, according to the age, expressed by the standard tables, and both muscular power and developmental progress, assessed on our provisional standards, also bear a definite relation to the other characters. But these children presented the

most diverse anomalies in the relationship mentioned. No order or specific pattern could be discerned and consequently, the series being a very small one and merely exploratory in nature, we noted the suggestions and laid the data on one side for the time being.

THE FIRST ADOLESCENT PUZZLE

During 1926 and 1927 we had examined a number of children between twelve and sixteen years who happened still to be of grade school rank. We paid no particular heed to these records at the time beyond devising from them a series of standards carrying our five to twelve-year-old standards upwards through puberty. We paid no particular attention to these records I say because, having already, in 1923, set up a provisional series of standards based upon the skeletons of adolescents in the laboratory we found our previously arranged observations fully confirmed by the studies on these living children.

It was, therefore, with considerable confidence that we took over another group of 800 children, this time drawn from Patrick Henry Junior High School, from whose headmaster, Mr. Taylor, and his staff we received the most courteous consideration. When, however, we came to arrange the data culled from Patrick Henry children we found ourselves plunged headlong into a quite unforeseen problem. The height and weight standards which we had devised on the adolescent Stearns Road children were quite outdistanced by the Patrick Henrys. Not only did we strike this scientific snag but the roentgenograms demonstrated at once that either the Patrick Henry children were, in general, accelerated in development far beyond Stearns Road children or our provisional standards of roentgenographic development during adolescence, based upon adolescent skeletons and confirmed by observations on adolescent Stearns Road children, were erroneous. This was a very serious check to the progress of our work and it was necessary to review the social and economic conditions in which these several groups of children found themselves.

Luckily for us the Developmental Health Inquiry had taken over the work originally financed by the Health Council and we possessed the necessary funds to enlarge our program. We immediately organized psychological and sociological units in the survey.

After a great deal of very patient concerted investigation it became evident that the new Patrick Henry standards were reliable for the assessment of developmental growth in adolescent children. The failure of the previous standards was due to the fact that they were devised partly from the study of Stearns Road adolescents stunted in growth, retarded in physical development and of low mentality, partly from observations on skeletons of adolescents whose development had suffered interruption or delay previous to their death. The reason why we had not noticed this in the original investigations is found in our early studies. It is this. When delay takes place in developmental growth the epiphysial progress in union is retarded as a whole pattern. The order of epiphysial union is not changed.

Later investigations demonstrated the existence of exceptional instances but, in general, disease and adverse socio-economic conditions are associated with

disturbances of developmental growth which express themselves in retarded or defective physical and mental progress.

THE SECOND ADOLESCENT PUZZLE

We had scarcely surmounted the difficulties of this first check before we were face to face with a second. In 1930 the Cleveland Press instituted a Health Contest for High School Children and invited the Developmental Health Inquiry to act as adjudicator.

The method of selection was the election by the children in each school of one boy and one girl to represent the ideal of what a boy or a girl of that particular life-period should be. No further directions were given. The students did not make their choice upon the basis of physical symmetry, mental attainment or even of popularity, though doubtless all these factors were subconsciously present in making the selection. My own preconceived notions received a severe shock when we examined the elected representatives. They were not at all the type of adolescents whom I would have chosen. But the instinct of the students was a safer one to follow. The results of our examination showed a quite unusual symmetry of developmental growth in dimensions, nutrition, physical progress towards maturity, mental attainment and emotional adjustment. In other words, these were children well rounded in all aspects of developmental growth.

Once again, however, the roentgenographic standards which we had devised, this time upon Patrick Henry children, proved inadequate. That is to say, these health contest students were advanced in development, as they were in height, weight and mental attainment, beyond the average. In height and weight the difference was equivalent to approximately a year's growth; in physical and mental development it was approximately the value of two years. These conclusions were confirmed by the second Press contest of 1931.

A NEW CLASSIFICATION OF CHILDREN

Putting together the results of our experience in the solution of these two adolescent puzzles we drew up a new scheme for classification of developmental growth.

(1) Average or mediocre group represented in height, weight, roentgenographic and mental development by the Patrick Henry series.

(2) Superior group represented by corresponding features in the Press Contest group.

(3) Retarded group comprising the defective children of Stearns Road and the dead children of the laboratory.

Our next task was obviously to explore groups of children in certain physiological and health relationships. We watched onset of menstruation and found the menarche coinciding with a roentgenographic assessment of the six months before the fourteenth birthday in skeletal development, whatever the chronological age. This relationship is not invariable, but so constant as to be clearly significant. We noted the retardations of hypothyroid children and the effect of thyroid medication, through the kindness of many Cleveland

physicians. We also contrasted the appearance of roentgenograms of diabetic children with and without insulin treatment through the generosity of Dr. Priscilla White of Boston.

In ways such as those just instanced we confirmed the conclusions already drawn, namely, that roentgenographic assessment is a fair indication of developmental progress and that disease constitutes a most serious handicap on development.

QUEERING THE START

I have mentioned the basis of roentgenographic assessment in adolescence as the union of epiphyses and I have shown how roentgenographic assessment between five and twelve years is carried out by noting the penetration of the epiphysial cartilages by bone. It still remains to demonstrate how assessments can be made in infancy and the preschool period. During the sixth month of fetal life a bony center appears in the calcaneus and in the last weeks of fetal life five other centers appear, namely, those for talus, lower epiphysis of femur, upper epiphysis of tibia, head of humerus and cuboid in that order. All these centers are present at birth in well developed, well grown children whose weight is 2,500 grams or more and whose stature reaches at least 480 mm. During infancy other secondary centers make their appearance, but the time-relationship on all schedules hitherto presented has been so erratic that it has been considered invalid as a measure of developmental progress. That is because our minds have been obsessed by the morphological doctrine of inherent variation. The more we study variation the more clearly we realize that variation is not inherent but induced.

A prolonged investigation of the skeletons of dead children demonstrated that the date of appearance of these secondary centers is related to health conditions. In all our dead children the retardation of epiphysial ossification was shown by Doctor Francis in 1929 to be determined by date of onset and severity of disease or dietetic disorder. We, therefore, set ourselves to establish a new schedule of epiphysial ossification upon living children whose medical, dietetic and growth histories were definitely known. From this study we found that centers appear in groups at definite dates and that if the child is ill at the time when a certain group is due to appear that group fails to make its appearance on time. The centers do indeed make their appearance later, how much later depending upon the severity of the handicap. Practically all secondary centers are visible in girls by two years and nine months and in boys between third and fourth birthdays. The sex difference does not begin to make its influence felt until towards the end of the first year. When it is apparent this seems to be an expression of difference in calcium metabolism rather than of a specific sex distinction. The available lime is deposited in the growing bones and the epiphyses. The more rapidly growing bones of boys seem to utilize so much of the available calcium that less remains for epiphysial ossification than in girls. It does not follow, however, that boys of small stature will show earlier epiphysial ossification than large boys for the smaller boys are usually children of inhibited developmental growth, another manifesta-

tion of handicap. This handicap shows itself in another manner which we had not foreseen.

Psychological tests are usually measures of skill of various types. In early childhood they can be divided into tests of muscular power, tests of muscular control and tests of social response. The two latter types involve experience; the first does not. Children handicapped in developmental growth show not merely a delayed epiphysial ossification but a deficient muscular power though in the lesser degrees and earlier stages of handicap the epiphysial centers alone may register the disturbance.

On the basis of these observations and deductions we instituted, in 1931, a detailed and comprehensive survey of developmental growth during infancy, starting with babies three months old. This required the addition to our organization of a dietetic service and of an experimental study of the mineral content and metabolism in diet. These parts of our program are still in their early stages, but we have already obtained significant impressions. They are the following, and from them we can devise a measure of developmental health in infancy.

(1) There is a time-schedule for the appearance of ossific centers in small bones of wrist and ankle and in epiphyses.

(2) The time-schedule is disordered by disease, by dietetic disturbance and by intermittent starvation resulting from defective socio-economic conditions.

(3) During convalescence and after the reestablishment of health, centers delayed in appearance during the handicapped period begin to ossify and sooner or later, according to the severity of the disturbance, make up for the time lost.

(4) If the handicap increases in severity until death supervenes the missing centers never appear.

ANTHROPOID GROWTH

The Inquiry was instituted in 1929 and was planned to continue five years. During so short a period it is plain that we could not survey and follow the entire period of human developmental growth from birth to adulthood. We, therefore, split the twenty years of human growth into lustra of five years each, organizing our observations on successive groups of children to cover the range of human growth in the allotted time.

Our conclusions would, however, still be inadequate unless counter-checked upon some mammalian form at least fairly closely akin to man and more directly under our experimental power than human children could ever be. Our earlier observations had demonstrated that primates differ from all other mammals in having a relatively long childhood, whereas they differ from man in having an exceedingly short adolescent period. For these reasons we decided to amplify our investigations on human growth by a collateral study of primate growth. For this purpose we added a Monkey Observation Station on a small scale and greatly increased the collection of skeletons of primates in the Hamann Museum by the accumulation of animals both wild-killed and after

confinement in zoological gardens. None of this material has been collected in the manner adopted by other scientific institutions. It is more economical and much more satisfactory to obtain salvaged material which would otherwise have been lost to science. Our collection of gorillas, for example, which comprises almost a third of all the skeletons and skulls at present housed in the collections of the world, has been entirely obtained by salvaging the skeletons of animals killed by natives in the African Bush. The money spent by us in purchase has gone toward the education of missionaries' children and the eradication of leprosy and sleeping sickness in West Africa.

The anthropoid reaches at about four years the stage of development attained by the human child at six. Thereafter the anthropoid matures with great velocity so that, by his seventh birthday he has passed the stage of adolescence and attained young adulthood.

We formed a close association with the Yale Anthropoid Station under Professor Yerkes and owing to his kindness and the generous cooperation of his staff we have begun to elucidate further many of the puzzling problems of human childhood.

I have mentioned, on an earlier page, the fact that Bolk discovered prematurely united sutures in man to be already closed at seven years. This is probably a survival of anthropoid character. It is matched by many other illustrative examples of similar nature, some of which have been published but most of which still lie recorded only in our files.

The views expressed on epiphysial ossification have been borne out on the study of Yerkes' living chimpanzees. The association of physical development as shown in the epiphyses with muscular power, muscular control and behavior progress have also been checked and confirmed in Professor Yerkes' laboratories.

Thus the study of primates and, more particularly of anthropoids, has become an integral and essential part of the investigation of human growth patterns.

THE BOLTON STUDY

In 1930, seizing the opportunity which this fast-growing survey of child development provided for the economical study of facial growth and orthodontic problems, Mrs. Chester Bolton and her son, Charles Bingham Bolton, provided the funds for a collateral investigation from the point of view of the orthodontist. This study is under the able direction of Dr. B. Holly Broadbent.

One of the far-reaching observations made twenty years ago by Boas was the demonstration of change in facial form in the children of alien immigrants to New York from Central Europe. This observation was matched by our discovery that young children suffering from chronic gastrointestinal disorder possess a very characteristic narrow pinched face.

This theme was prosecuted upon the skulls of our dead children housed in the Laboratory of Anatomy and became the starting point for an investigation, under the Bolton Study, of facial development.

Dr. H. C. Rosenberger joined our staff in 1931 and commenced to investigate the development of the upper respiratory passages and has already

attained striking results upon the maintenance of free air-way and the production of adenoids.

Doctor Broadbent and his staff have demonstrated in quantitative manner the story of facial growth and the relation thereto of dental development, eruption and occlusion together with the effects of health handicaps. This study is most significant for the future of orthodontia in particular and of medicine in general. Publication of their results is proceeding as fast as leisure to write permits.

BRAINS

For twenty years we have been collecting the brains of known individuals, both adult and child, whose bodies have come into our care and the records of whose life and last illness are in our hands.

In 1930 Doctor Loo, after an apprenticeship of four years under Prof. C. Judson Herrick of Chicago, undertook a survey of the children's brains and discovered to our complete surprise that, all through earlier childhood at least, the developmental growth of the brain can be followed with the same meticulous precision as I have shown to be possible in the skeleton.

For the first time it becomes possible to correlate actual developmental growth in brain with the increase in skills and mental capacity. Much time and labor must be devoted to this aspect of the work before clarity can be attained similar to that we now have on skeletal progress. But the association in the Inquiry of an experienced psychologist, Dr. Dewey Anderson with the physicians and anthropologists of our combined staff, renders this prospect secure in the end.

The investigation must first master the details of development from birth to six years when brain growth is approximately complete and mental development undergoes a profound change. The later phase of the work must deal with the progress in developmental growth and the satisfaction of skill-hunger in later childhood and adolescence.

It is now abundantly clear that the brain, so far from being immune to disaster as was formerly thought, is vulnerable to disease, dietetic disorder and socio-economic privation as are other parts of the body.

Thanks to the cooperation of the Girls' Bureau of Cleveland we have been already able to investigate, in a preliminary manner, the handicaps of the adolescent. I have mentioned the fact that mentally retarded children in Stearns Road School are also generally physically handicapped in developmental growth.

The adolescent phase of this study, as illustrated at the Girls' Bureau, is of a different order, but none the less significant in community welfare. These girls suffering social and domestic infelicity are usually physically developed beyond their years, but display a developmental disharmony in mental retardation which leaves their skill-hunger unsatisfied, so that they seek compensation in such skills as they are capable of atttaining. There is no more impelling urge for the continuation of the work upon which we are engaged than this misdirection of skill-satisfaction.

THE WHITE HOUSE CONFERENCE

No more stimulating encouragement or more timely expression of confidence could have been given to the Inquiry than its inclusion in the constructive work of the White House Conference of 1930-31 when the Committee reports upon skeletal growth and development and of physical status were assigned to us by Dr. Kenneth D. Blackfan, chairman of the Committee on Child Growth and Development. Not only were those topics confided to our care but the Conference provided funds necessary for the elaboration of data needed for their effective presentation at a date earlier than we could otherwise have hoped to bring them into order. It was this action of the White House Conference which set the Inquiry upon a research basis secure enough to justify the rapid progress which has been possible in the short period of its existence. Gathered into those Committees and spread upon the White House records were the authoritative evaluations of our present knowledge and our future needs. Those who took part in the preliminary discussions and assisted in drawing up the final reports accumulated a wealth of knowledge and grasp of essentials which, dispersed as it now is over the country, must influence for human betterment, the welfare of children throughout the nation. This record of our progress and present achievement would be lamentably inadequate without proper acknowledgment of the benefit derived by the Inquiry from its graceful recognition by that great constructive device for the children's welfare, the third White House Conference.

QUANTITATIVE MEASURES OF HEALTH

At this stage it is well for us to review the progress made by the Inquiry too date.

(1) In amplification of the criteria hitherto utilized in the assessment of child development, namely chronological age and measures of height and weight, we have been able to devise quantitative determinations of actual bodily development by the roentgenographic record of skeletal progress toward maturity.

(2) These roentgenographic standards have been checked against functional indicators of bodily development and found satisfactory.

(3) By this method of quantitative assessment the effect of disease, of debility and of privation have been quantitatively registered.

(4) The observations made on children have been checked upon primates in health and disease and shown to be valid.

(5) A correlation of physical development in health and debility has been made with mental and emotional growth and with behavior and this again has been checked against similar studies on anthropoids.

(6) The further elaboration of the studies mentioned in the last paragraph and others on diet are now being actively pursued.

(7) A practical demonstration of the validity of the methods of the Inquiry as a quantitative measure of health progress is in full swing, encouraged and supported by the medical profession of Cleveland, and

carried out by the cooperation and faith of the parents of Cleveland's children.

THE ACTIVE DIRECTION OF DEVELOPMENTAL GROWTH

To complete this report allusion must be made to the very significant studies on developmental growth in their experimental aspect being carried on by Doctor Zuck and others of our staff.

Hitherto investigations upon bodily metabolism, especially as it is related to diet and to the endocrine functions, have been limited in their registration to measures of weight and general well-being. The quantitative methods of the Inquiry have given us a new and far more reliable measure of effectiveness. No claim is made for the establishment of new means whereby developmental growth can be controlled, stimulated or repressed. But the work already carried out demonstrates our ability to measure the effectiveness of our treatment, or at least of the progress made during treatment. It enables us to compare the results with the progress made by other children under similar conditions but without treatment. The adjustment of developmental growth by the methods just outlined is no longer a treatment carried out cautiously in hope but without effective control. Whereas former workers have estimated the effects of that treatment, the Inquiry has devised methods of accurately measuring the effects, so that physicians in future will know what they are doing, adjusting dosage and vigor of stimulation in full understanding of the results produced.

In order to understand more clearly the principles of mineral metabolism which are involved in these methods of treatment we have had to develop a plan of experimentation with animals and biological assay in vitro upon which Doctors Zuck and Venar are engaged. These investigations are based on the work of Robison, Howland and Shipley and require the application of micro-chemistry to the problems of calcification and ossification in cartilage and bone. There is good reason to expect that our understanding of the deposit and mobilization of calcium will be clarified by the incorporation of this work in a general study of changes undergone in the skeletons of normally and abnormally developing children rather than as experiments isolated from clinical study and interpretation.

This phase of the work is still in its infancy. Before the termination of the Inquiry we confidently expect to see great progress in the power of medicine to foster and adjust developmental growth where it has become handicapped from any of the causes outlined on earlier pages. This is one of the most constructive and practical contributions which the Inquiry has been privileged to make to medical science.

JEOPARDS

Cleveland is most fortunate in having upon the Health Council Mr. Howard Whipple Green, whose recent study of Census Tracts has enabled the Inquiry to take full advantage of the opportunity created by Mr. Green's study for assessment of the social conditions in which the children of this city live.

By the cooperation of organizations like the Board of Education, the Maternity Hospital, the Babies' and Children's Hospital, the Western Reserve Nursery School and the Day Nursery and Free Kindergarten Association we are in a position to investigate developmental growth as demonstrated in the different social grades and phases of economic security found in an urban population.

To attempt this comprehensive investigation on a basis of physical development alone would be clearly inadequate for the results could not be analyzed with that confidence, precision and completeness necessary to transform the investigation into a scheme for human betterment such as Doctor Brush originally envisioned. It was for the purpose of properly transforming the study into a creative project of practical value that we developed first a psychological research and then arranged for the supervision of the sociological aspects of our work. As I have already noted the dietetic side of the investigation is now in process of elaboration and in 1930 we established an experimental phase for the utilization of animals and the medical direction of developmental growth in such defective human children as would add to our understanding of the problems before us.

It was not planned that these different phases of the study should be merely of a recording nature. Each is established on a basis of creative research to devise quantitative measures of registration for a thorough assessment of developmental health and progress in children and the conferment upon medicine of an instrument of precision available for the periodic health examination to which all communities are looking today.

In the summer of 1934 this Inquiry closes for its funds will then be exhausted. And, unless a new lease of life be granted the Inquiry by the settlement upon it of fresh financial resources, 1934 will see its definite termination. For the welfare of all children it may be hoped that some organization will be inspired to continue the work set up with such care and productive of such far-reaching results. It has shed new light upon the problems and difficulties of childhood, given help toward their alleviation and conferred an instrument of quantitative measurement and directive power upon medicine in the serial health examination.

THE FUNCTIONAL AND STRUCTURAL EVOLUTION OF THE VERTEBRATE KIDNEY*

HOMER W. SMITH

In outlining my subject for this evening I have gathered a miscellany of threads from comparative anatomy, physiology, biology and physical chemistry, for the purpose of weaving together the functional and historical story of the kidney—the chief excretory organ of the vertebrates. It has been necessary to confine myself to the general outlines of this story, and to avoid, as far as possible, the discussion of technical details; and for this reason I may appear at times to be jumping from theoretic peak to theoretic peak like a scientific mountain goat, but I can assure you that no one is more nervous about the gaping chasms that lie between the too distantly separated experimental facts than I am.

Prof. A. B. MacCallum remarked many years ago that the history of the earth is not written in the rocks alone; he was referring, as you may recall, to the salt composition of the blood, but his remark is equally applicable to the structure of the kidney; for the great geophysical changes that have produced a succession of vertebrate forms have also, we believe, left their imprint in the softer tissues of the chief excretory organ.

If we date the origin of the vertebrates at the opening of the Ordovician, and the origin of the Amphibia at the close of the Devonian Periods, then for 200 out of the total of 500 million years of its evolutionary history the vertebrate stem had fins and gills, and lived in water. If we consider the Amphibia as essentially aquatic animals and, therefore, date the true beginning of terrestrial life with the appearance of the reptiles at the opening of the Triassic, then for 300 out of the 500 million years, or for three-fifths of its total evolutionary history, the vertebrate stem lived in, or was bound down to, an aquatic environment. It is not surprising, therefore, that the anatomical and physiological characteristics of the kidney reflect this historical fact.

For this reason we can best begin the discussion of the evolution of the kidney by considering the circumstances of the ordinary teleostean fishes which live in fresh or salt water. The fish that lives in the fresh waters of an inland lake or river, and the fish that lives in the briny sea, resemble each other in respect to chemical composition and, as is well known, the blood has about the same osmotic pressure and salt composition in spite of the great diversity of their environments. This constancy in regard to salt composition and osmotic pressure is truly a physiological "steady state," in Claude Bernard's sense of the term; it results from compensatory activities constantly operated by the organism in order to maintain it. In Figure 1 I have drawn a fresh-water teleost on the left and a salt-water teleost on the right. I have indicated the difference in osmotic pressure of the environment by shading, the dark medium representing the sea water of high osmotic pressure, the light medium representing fresh water of low osmotic pressure; an intermediate shade in the

* A lecture given before the Rutgers Chapter.

body of the fish indicates an intermediate osmotic pressure in the body fluids of the organism. In fresh water the teleost is osmotically superior to its environment, while in salt water the teleost is osmotically inferior to its environment. Let us suppose for a moment that all compensatory physiological activities were suspended, and that the fish were merely a passive osmometer.

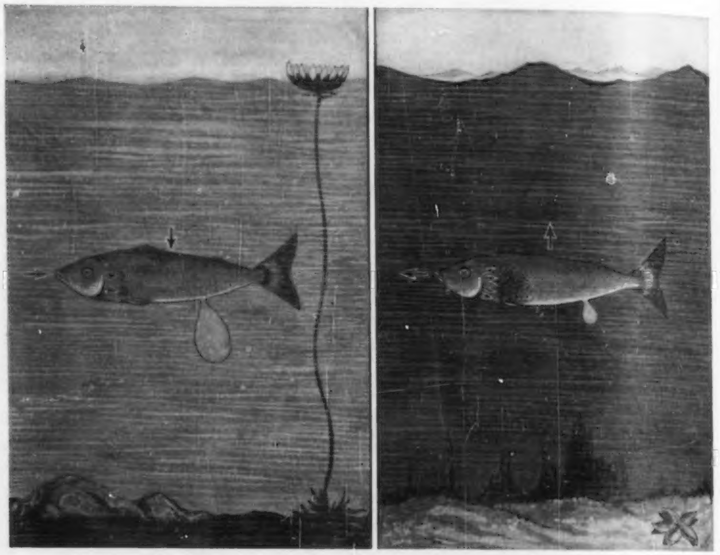

FIGURE 1

Because of the existing osmotic gradient the fresh-water fish would absorb water through its skin, its oral membranes and its gills, and it would tend, therefore, to become swollen and osmotically diluted by this absorption of water until it was infinitely expanded, a process that could end only in ultimate dissolution. The salt-water fish, on the other hand, would lose water through its skin, its oral membranes and its gills, and it would, therefore, tend to become correspondingly concentrated by the abstraction of water until it was reduced to isotonicity with the sea water in which it was immersed; although such a state of osmotic concentration is theoretically possible, we know that death would result in the teleost before that end was reached. Not only does the environment tend to extract water from the body at every point of contact, but in so far as the fish accidentally or deliberately swallows any of the sea water, it must absorb the greater part of the ingested salt as well as the water from the intestine, and consequently the body becomes enriched relatively more with respect to salt than with respect to water, so that the net result is precisely the same as though water had been extracted through the skin.

It is obvious that to compensate for these passive osmotic movements the fish in fresh water must excrete from the body an excess of water over salt, and thus resist dilution; while the fish in salt water must excrete an excess of salt over water and thus resist concentration. Thus we may say that the fresh-water fish is faced with the task of *hypotonic* excretion and the salt-water fish with the task of *hypertonic* excretion; that is, the organism in fresh water must excrete at some point a fluid which is hypotonic to the body fluids, while the organism in salt water must excrete a fluid that is hypertonic to the body fluids, if both are to maintain a steady state in respect to the composition of their body. Although space does not permit a review of the experimental methods and observations by which this problem has been solved, the salt and water cycle of the fresh-water and marine fish can be described briefly.

more H_2O than Salts

more Salts than H_2O

The fresh-water teleost excretes large quantities of urine which is hypotonic to the blood, as is indicated by the large size of the bag attached to a catheter inserted in the urinary papilla. In addition—and what is a most important observation of this connection—the greater part of the salts derived from ingested foods are not excreted by the kidneys, as is the case in the higher animals, but by the gills. This branchial excretion of salts is indicated in the figure by the arrows around the operculum.

In salt water, in order to get any water whatever for the formation of urine, the fish must first drink sea water and absorb the water and salt from the gastrointestinal tract; then, once in the body, these two are handled exactly as in the fresh-water fish; that is, the salts are excreted by the gills and the water is used for urine formation. Thus the fresh-water and salt-water fish differ in their situation in that pure water is freely available to the one, and most of the water for urine formation is passively absorbed from the environment; while the salt-water fish can obtain water only by drinking sea water and absorbing the water and salts from the gastrointestinal tract. The two organisms ultimately use the same physiological operations to solve their problems, for both excrete most of the salt by way of the gills and most of the water by way of the kidneys, but quantitatively there is an important difference: water for urine formation is a relatively simple and inexpensive commodity in the fresh-water fish since it is freely available and there are no salts to be handled incidentally, while in the marine fish it is a very expensive commodity because the salts dissolved in the sea water must be secreted from the body again, secreted from a low osmotic pressure in the blood to a high osmotic pressure in the sea water which bathes the gills, and this secretory process against an osmotic gradient involves the performance of a large amount of physical-chemical work. It is not surprising to find, therefore, that in the marine fish the renal excretion of water (urine flow) is reduced to very low levels. In fact, in the normal marine fish the urine flow is only 1 to 5 percent of what it is in a fresh-water fish. This fact, I think, is a central one for the interpretation of the structure of the kidney in fresh-water and marine forms.

In passing it may be noted that the branchial secretion of salts which I have described has been confirmed and studied further by Ancel Keys, who believes that he has identified the cells in the gills which are responsible for salt secretion. These salt-secreting cells bear a remarkable resemblance to the hydro-

chloric acid-secreting cells in the gastric mucosa. Keys has made the interesting calculation that per gram of tissue, the gills of the common eel, Anguilla, can do as much osmotic work in this process of secreting salt against the osmotic gradient of sea water as can the mammalian kidney in reabsorbing water against the osmotic pressure of the substances normally contained in the urine.

It is also interesting to note that, so far as is known, it is only in these two places in the entire vertebrate kingdom—in the gills of fish and in the mammalian kidney—that osmotic work in the form of hypertonic secretion can be performed. The differences between various species of fish have not been extensively studied, but it is not an idle speculation to suppose that whether or not a fish can live in the briny sea depends in part upon whether it likes the taste of salt water well enough to drink it.

From a physiological point of view, the central feature in this problem so far as the kidney is concerned, is the osmotic limitation of that organ in the lower vertebrates. All vertebrates from the elasmobranch fishes, and probably from the cyclostomes, up to and including the mammals can excrete a urine which is hypotonic to the blood; but only the mammals can excrete a urine which is hypertonic to the blood. The processes of hypotonic and hypertonic excretion appear to be independent physiological processes referable to independent anatomical machinery in the kidney, and to have been independently acquired in evolution. There is, in fact, considerable evidence to support the view that hypertonic excretion in the mammals is a function of the loop of Henle which first appears fully developed in mammalian kidney (a segment corresponding to it is developed in some tubules in the birds' kidney, although the birds cannot excrete a hypertonic urine). This osmotic limitation is, I think, the important feature which has determined the structure of the renal unit throughout the vertebrates.

In order to bring a number of isolated facts into a coherent story it is necessary for me to proceed from this point in terms of some theory of the evolution of the kidney. If we examine a typical renal unit as observed in man or the dog (Figure 2) we find that it consists of a glomerulus in which a process of filtration is effected by the hydrostatic pressure of the blood; the filtered fluid then passes through a proximal convoluted tubule, then through the thin limb and thick limb of the loop of Henle, then through the distal convoluted tubule, and then into a collecting duct from which the fluid is led into the urinary bladder. During this passage along the tubules, chemical changes are effected upon the glomerular filtrate, some of which consist of the reabsorption of valuable constituents and some of which consist of the further secretion of waste products, so that the urine ultimately differs a great deal in its composition from the plasma from which it is formed. It is believed that in man about 90 c.c. of filtrate are formed in the kidneys every minute, of which 89 c.c. of water are reabsorbed by the tubules, leaving only, on the average, 1 c.c. of urine to be excreted, even under conditions of relatively high urine flow. Variations in urine flow are referable primarily to variations in the amount of water reabsorbed rather than to the variations in the amount of filtrate formed.

Our problem is, in part, to determine how this renal unit in man has been evolved and how it compares with the renal unit in other vertebrates. To do this we must go back to the earliest vertebrates of Silurian times. Thirty years ago most biologists held the view that the vertebrates had been evolved in the stable waters of the sea, and that it was as highly organized forms fitted for swift and powerful motion that they had penetrated into the fresh-

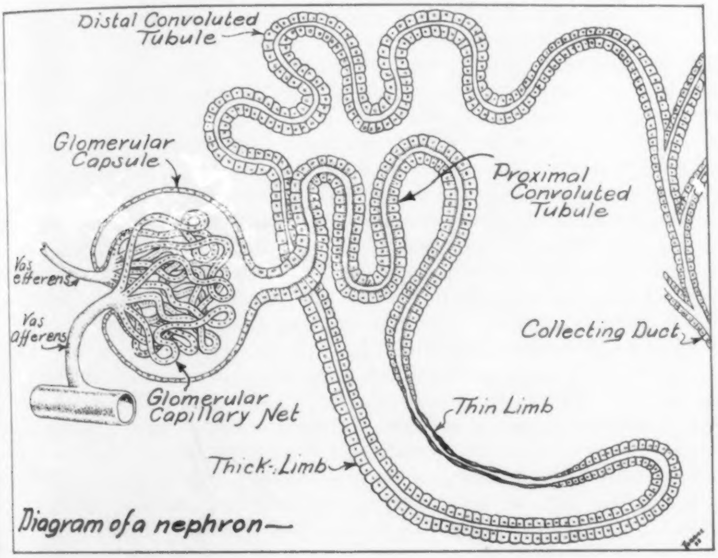

FIGURE 2

water rivers and lakes of the continents; but in recent years the nature of the fossiliferous beds in which the skeletons of the first fishes are found has led many paleontologists and biologists to revise this view. These beds are now generally interpreted to be of fresh-water origin. Chamberlain, as long ago as 1900, suggested that the first fishes were inhabitants of fresh water, and this view was elaborated with great care by the late Joseph Barrell. From Barrell's work, from the observations of Kiaer on the ostrocoderms of Norway, Stensio on the Lower Devonian fishes of Spitzbergen, and from many other lines of evidence, it may be set forth as a plausible, though not fully substantiated thesis, that the early vertebrates, at the time when the kidney was being given its definitive character, were inhabitants of the continental rivers and lakes and only secondarily migrated into the sea from this ancestral, fresh-water home. The present physiological and anatomical characters of this organ seem to be explicable only on this view. A few years ago Doctor Marshall of Johns Hopkins and myself attempted to interpret the structure of the kidney in terms

of this paleontological theory. We were primarily interested in the now well-known fact that in many marine fishes the renal unit lacks entirely a glomerulus, the tubules ending blindly like a rubber-finger cot. The number of such aglomerular fishes known has been increased in the last few years, and now totals about thirty species, and our knowledge of the comparative anatomy and physiology of the aglomerular kidney is being enriched by the studies of Marshall, Grafflin, Edwards, Bieter and others.

It is supposed that the invertebrate form from which the vertebrates were derived possessed a tubular kidney opening perhaps by means of a nephrostome into the coelomic cavity or the pericardium; in short, a kidney much like that which is observed in the majority of invertebrates living today, and in the embryonic kidneys of some vertebrates.

Just when or why this hypothetical invertebrate, which was destined to be the ancestor of the great vertebrate class, migrated from its primeval home in the sea to the fresh waters of the continents, there is no knowing, but we may safely speculate about the physiological consequences of that migration; the organism carried with it a blood of relatively high salt content reflecting its physiological adjustment to its previous life in sea water, and for this reason it was superior osmotically to the new environment in which it found itself. There was consequently a persistent influx of water into the body by simple osmotic absorption just as in the case of the fresh-water fish, and this influx of water needed to be corrected by some device capable of excreting large quantities of water in an economical way. It is supposed that the device for this purpose, as ultimately perfected, consisted of the glomerulus whereby the blood-vascular system was brought into close juxtaposition with the tubule, and whereby large quantities of water could be excreted by the simple expedient of filtration at the expense of the hydrostatic pressure of the blood. Thus we consider the glomerulus to be an adaptation to life in fresh water. So long as the organism remained in fresh water (dipnoans, ganoids and teleosts) or in intimate dependence upon it (Amphibia) we would expect the glomeruli to persist and perhaps to be improved upon; but with the secondary assumption of a marine habitat (marine teleost) where the osmotic gradient was reversed and where water needed to be conserved, or with the assumption of terrestrial life in which water conservation became an absolute necessity (arid-living reptiles, the birds and the mammals) the organism could no longer use the primitive water-excreting mechanism, as represented by the glomeruli, economically, and there was thus a need to either (a) discard them, or (b) amend their primitive function by adding distally a new mechanism which was capable of reabsorbing the valuable filtered water while yet discarding the salts. The first process (the abolition of the glomeruli) appears to be occurring in the marine teleosts, and perhaps in the reptiles and birds. The second process (the addition of a "water reabsorber") has occurred in the mammals and perhaps is occurring to some extent in the birds.

In the primitive fishes we find large and numerous glomeruli; these glomeruli are highly vascular, delicate in structure and show every evidence of being highly efficient as a filtering mechanism. The same is true of the Amphibia. Neglecting for the moment the story in the elasmobranch fishes and passing

on to the marine teleosts we find that in these the number of glomeruli is greatly reduced, the size is reduced and the glomeruli tend to become invaded with inert epithelial or connective tissue. That this reduction in number, size and delicacy represents a step in the process of evolutionary disappearance I think no one can doubt, because the end-result is beautifully demonstrated in the aglomerular fishes where not a single glomerulus persists. Among the more familiar aglomerular fishes are the goose-fish (Lophius), the toad fish, sea horse, pipe fish, and nearly all of the deep-sea fishes so far studied. The fact that a fish is a deep-sea fish may be interpreted to mean that it has been a resident for a great period of time in the sea and has migrated far away from its ancestral fresh-water home, and it is to be expected that they would, therefore, show the greatest change in renal structure. In Lophius a few glomeruli are observed in young fish, but these become detached from their tubules in the adult and lose entirely their functional capacity. Recent investigations of Grafflin (unpublished) show that in the daddy sculpin glomerular degeneration is present, but incomplete in young specimens, and advances with age so that in old specimens not a trace of glomerular function can be detected by physiological tests.

To summarize what I have said thus far, the essential physiological problem is this: that because of the hypertonicity of the sea water in which the marine fish lives, the excretion of urine is a very costly affair and consequently it is reduced to a minimum; where a fresh-water fish excretes as much as 200 c.c./kg./day a marine fish normally excretes only from 2 to 5 c.c./kg./day. From the comparative anatomy, the embryology and the paleontology of the vertebrates we infer that this oliguria in the marine fish, as compared to its fresh-water ancestors, is intimately related to the progressive degeneration of the glomeruli. Of course, it cannot be argued that the glomeruli are disappearing simply from lack of use, because not even a renal physiologist would venture to suggest such a direct and causative relation between function and evolution. But it can be asserted with confidence that, on the one hand, the organism in the sea cannot efficiently use its glomeruli and, on the other hand, that the glomeruli are disappearing in large numbers of marine species, and that some species have been reduced completely to the aglomerular state. Here is a new problem inviting a test of the mutation theory.

That the aglomerular condition is not a transient adaptation goes without saying, but we fortunately have more concrete evidence to justify our speaking of the disappearance of glomeruli as a true evolutionary process. While in Siam three years ago we studied the fresh-water pipe-fish which breeds, lives and no doubt has completely adjusted itself to a fresh-water habitat in comparatively recent times, after its kind had sojourned in the sea for countless years. The fresh-water pipe-fish is aglomerular like its marine brothers, bearing out the thesis that once the glomeruli have disappeared they cannot be regained except to start at the beginning again, and evolve a wholly new and probably somewhat different type of filtering bed. Perhaps this could be done, but it is asking a good deal of even the versatile vertebrates.

Returning now to the reptiles and the birds, it would be expected that glomerular degeneration would likewise be evident in these forms, since in their

evolutionary history they also left a fresh-water habitat for a life on land where water was at a premium. No aglomerular reptile or bird has yet been found, but it is significant that the glomerulus in the arid reptiles is reduced in size and very poorly vascularized; in addition it contains a dense core of connective tissue which must diminish its efficiency as a filtering device. In the bird the glomerulus is small and poorly vascularized, as in the reptile, and it possesses a core of what some investigators interpret to be connective tissue, but others interpret to be persistent embryonic cells. The mammals, on the other hand, have kept the glomeruli and used them efficiently by incorporating in the tubular portion of the kidney an efficient water-reabsorber (the loop of Henle). Thus they have done again in the kidney what has been done so often in other parts of the body; that is, put an old and otherwise vestigal organ to a new use. By reabsorbing 99 percent of the water which comes through in the glomerular filtrate they have converted the old and relatively simple filtration system into a more complex filtration-reabsorption system. We cannot yet say whether the mammalian system possesses advantages over the primitive system, but every biologist will agree with me, I think, that organs are as likely to be determined in their form by evolutionary history as by considerations of efficiency.

The principle of putting old things to new uses is exemplified by another notable instance in the elasmobranch fishes, the sharks, rays and skates, in which the waste product, urea, has been deflected to an osmotic rôle.

It will be recalled from what was said about the marine teleosts, that they face a constant water hazard by living in the sea. The urine which they excrete is gained from their environment at the expense of considerable physiological work; and any injury to the skin whereby the escape of water from the body is facilitated requires that they drink more water and excrete more salts in order to compensate for the resulting dehydration. Inherently, the battle for life in the ocean is perhaps no more arduous in the physical-chemical sense than the battle for life in fresh water, where the environment tends constantly to seep in and to dilute the organism to the point of physiologic dissolution; but there is this difference: urine excretion, though primitively, perhaps, a device for the regulation of the water content of the body, is secondarily a device for the excretion of metabolic waste products, and in this respect the fresh-water fish with an abundance of water available to it is in a superior position to the marine fish which is physiologically limited to a low urine flow.

When we turn to the second great subdivision of the fishes, the elasmobranch fishes, we find an extraordinarily interesting adaptation to circumvent these difficulties. It has been known for many years that the elasmobranch fishes normally contain large amounts of urea which permeates the blood and tissues. This substance is the typical end-product of the combustion of protein nitrogen in all vertebrates except the birds and reptiles. But by most of the vertebrates, including the teleost fishes, it is excreted as fast as it is formed.

The gills of the teleost are freely permeable to urea so that it diffuses from the blood into the surrounding water, and such of it as is not lost in this

way is excreted in the urine (Figure 3). The gills of the elasmobranch fishes are relatively impermeable to urea and, in addition, the kidneys of these animals conserve this substance by reabsorbing it from the glomerular filtrate. The result is that urea accumulates in the body until it reaches a concentration exceeding that found anywhere else in the animal kingdom—from 2 to 2½ percent by body weight. The result of this physiological uremia is, of course,

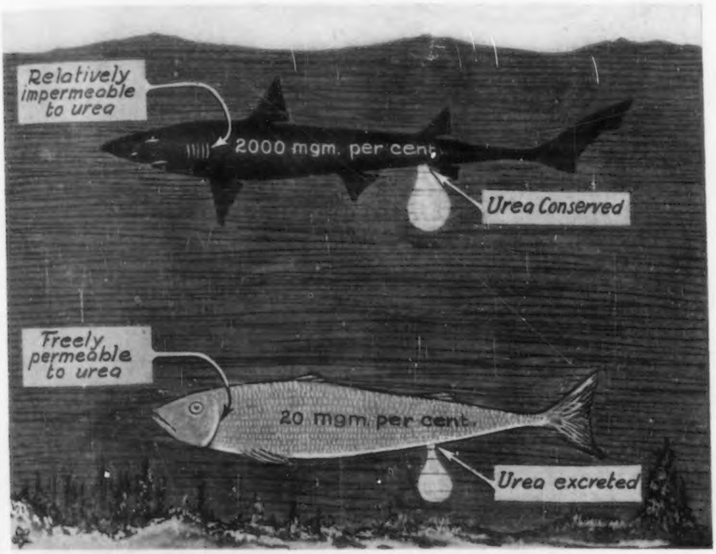

FIGURE 3

to raise the osmotic pressure of the blood. Actually, the conservation of urea is carried on to such an extent that the osmotic pressure of the blood of the marine elasmobranchs is greater than that of the sea water in which they live. These facts are illustrated diagrammatically in Figure 4, where our familiar fresh- and salt-water scapes are superimposed over a cartesian graph relating the osmotic pressure of the blood to the osmotic pressure of the external medium.

It will be seen that the shark in fresh water resembles the teleost in fresh water in that they are both osmotically superior to their environment and, therefore, tend to absorb water by a natural osmotic process and have no need, and in fact do not, normally swallow it. The marine teleost, as we have seen, because the sea water tends to extract water from the body, must drink the sea water and excrete the ingested salts by way of the gills in order to get water for urine formation in compliance with the osmotic limitation of its kidney, but in moving from fresh into salt water it suffers little change in the osmotic pressure of its blood. The marine elasmobranch, through raising the osmotic pressure of its blood (by the conservation of urea) to a level above that

of its environment, maintains itself in qualitatively the same position as its brother in fresh water; it is osmotically superior to its environment and can absorb water for urine formation directly, to a small extent though the skin, but to a larger extent through the gills and oral membranes, without the necessity of drinking any of its briny habitat.

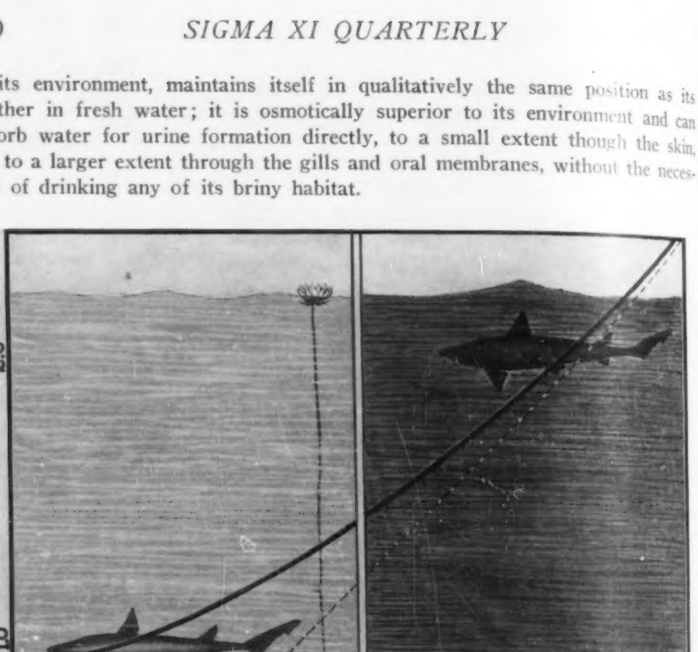

FIGURE 4

The net result is that the urine flow in the marine elasmobranch is several times greater than in the marine teleost, and it is significant that no aglomerular elasmobranch has yet been found and that, in general, the glomeruli in these forms do not show the evidence of degeneration that is observed in the teleostei.

Since elasmobranch fishes constitute a subclass of extreme antiquity we may believe that the conservation of urea whereby an old thing is put to a new use constitutes a physiological discovery of equal antiquity. It is interesting to note that the elasmobranch fishes are either viviparous, or the egg is laid in a cleidoic, or impermeable, case, and I am inclined to interpret this fact as a concomitant of the urea habitus, since it is necessary to conserve the urea in the embryonic as well as the adult condition. The elasmobranch tubule pos-

sesses a segment which is not present in any other subclass of vertebrates, and which we infer is responsible for the reabsorption of the urea, a substance that is handled as a waste product by other forms.

The putting of old things to new uses is, of course, one mode of evolution. If we could return to this discussion 100 million or 200 million years hence, we might find the renal glomerulus, primitively designed to filter water out of the body, secondly, extroverted to the outside and turned into a secondary sex character, a luminescent organ, or into some other functional freak of nature, to the delectation of those who see in evolution merely a record of biological activity and experience, rather than a progressive movement towards some far-off, divine event.

CHAPTER REPORTS

The following chapters and clubs have submitted reports of their activities for 1932-33:

Chapters		*Clubs*
Worcester	Case	Alabama
Northwestern	North Carolina	Buffalo
Kentucky	Pennsylvania State	Arkansas
New York	Minnesota	Texas Technological
Rensselaer	Lehigh	West Virginia
Michigan State	Pennsylvania	Oklahoma A. and M.
Rochester	Yale	California at Davis
Oklahoma	Arizona	Carleton
Missouri	Western Reserve	
Johns Hopkins	Cornell	
Virginia	College of Medicine, U. of Illinois	
Maryland		
Stanford		

The above lists represent about 40 percent of the chapters and 25 percent of the clubs. The National Secretary will present a summary of the reports to the Convention. Chapter and club secretaries who have not already done so are asked and urged to submit reports. If these are received in the office of the National Secretary by December 20, they will be included in the résumé of chapter activities which will be placed in the hands of delegates at Atlantic City.

AN APPRECIATION OF JULIUS STIEGLITZ

At the meeting of the American Chemical Society in Chicago last month Prof. Julius Stieglitz was highly honored by several hundred friends and associates who gathered at dinner and reviewed his distinguished career. All present responded heartily and appreciatively to the different speakers who reviewed the long record of his splendid service.

The occasion was more than ordinarily significant to those members of Sigma Xi who recalled his significant work as national president of that organization to which office he was elected in December, 1916. The four years of his incumbency marked significantly a transition from older times to present-day conditions. Sigma Xi had grown to embrace thirty chapters. The old order of things had proved inadequate for the proper handling of so large and widespread an organization. Officials had been working for some years on a revision of the constitution and the reorganization of methods of procedure. As chairman of this important committee, Professor Stieglitz presented that year an extended report characterized by a conception of the enlarged opportunities which lay before the organization in which he emphasized the need of vigorous and united activity. The report was drawn up in a fashion characteristic of the career and achievements of the man and commanded immediately the vigorous support of the convention and of the entire organization.

That time was, furthermore, a period of intense activity in which the attention of scientific men as well as of all others was irresistibly diverted from many important situations by the problems presented by the World War. The 1918 Convention of Sigma Xi was necessarily postponed, but under the leadership of President Stieglitz the relations of the Society to scientific activity and its emphasis upon the needs of research was maintained and even increased.

The reorganization of the Society was completed at the 20th Convention in December, 1919, which was held in St. Louis. At that time he turned over the leadership of the organization with an inspiring address which pointed out clearly the new opportunities offered by the new constitution and in the period of reconstruction just opening. At that time the first Sigma Xi club was officially organized. The new chapter at the Mayo Foundation opened an avenue for the development of the Society which emphasized its relation to research and its readiness to depart from narrow constructions and ancient limitations.

Professor Stieglitz's tributes to our first president, Henry Shaler Williams, as printed in the September, 1918, QUARTERLY and to Samuel Wendell Williston, published just after the close of the war, are not simply inspired tributes to some of the great workers of the Society but are noteworthy examples of his appreciation of the spirit of Sigma Xi and of his vision of its future.

A SMALL CHAPTER AND A LARGE WORK

The Swarthmore Chapter, which since its installation has made an annual contribution to the National Society in support of research, announces a Swarthmore fellowship for research to be awarded in the spring of 1934. The fellowship will carry a stipend of $1,000, and the award will be made to an associate of the chapter who has become a graduate student of outstanding ability.

Holders of the fellowship will make informal reports to the chapter on the progress of their work, and at the expiration of the fellowship will present a formal statement at a public meeting of the chapter.

Applications for the Swarthmore fellowship must be made on forms provided by the secretary of the chapter and must be submitted not later than February 15, 1934.

IN MEMORIAM

MRS. LOUIS B. WILSON

The sympathy of the entire membership of Sigma Xi is extended to our President, Dr. Louis B. Wilson, in the great bereavement that has come to him in the death of Mrs. Wilson, which occurred in Rochester, Minnesota, on the morning of November 6. Mrs. Wilson had been ill for some time but kept bravely at her important task as editorial worker in the famous Mayo Institute, whenever and as long as her indomitable spirit could overcome the great drain on her physical strength which a devastating disease was constantly making. She was connected with the Institute since 1907 and developed a library and editorial work in connection with the publication of scientific papers by members of the staff. She was well known in her field and her ability was recognized by the most prominent physicians in this country and in Great Britain.

SIGMA XI CLUBS

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Colorado Agricul. College	C. Rohwer		H. E. Brewbaker	H. E. Brewba
University of South Dakota	E. P. Rothrock			
Louisiana State University	E. C. Timms	A. D. McKinley	W. Whitcomb	W. Whitcomb
University of Alabama	J. O. Foley	Marie C. D'Amour	T. N. McVay	Anna Church
University of Arkansas	L. C. Price		L. M. Turner	L. M. Turner
University of Calif. at Davis	P. W. Gregory		F. A. Brooks	F. A. Brooks
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Bucknell University	W. H. Stewart		J. S. Gold	J. S. Gold
Buffalo	G. H. Cartledge		W. L. Tressler	W. L. Tressle
Oklahoma A. and M. College	W. A. Craft	J. H. Cloud	J. E. Webster	J. E. Webste
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North Dakota Agr. College	L. R. Waldron	D. S. Dedrick	C. I. Nelson	C. I. Nelson
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